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Claims

We claim:

1. A method of inhibiting intimal hyperplasia in the vasculature of a mammal, comprising:

administering to said mammal an antihyperplastically effective amount of an anti-platel t derived growth factor (PDGF) receptor antibody.

2. A method according to claim 1, wherein said antibody inhibits one or more intimal hyperplastic processes selected from the group consisting of vascular smooth muscle cell proliferation, vascular smooth muscle cell migration, and neointimal deposition of extracellular matrix.

3. A method according to claim 1, wherein said antibody inhibits binding of PDGF to PDGF receptors.

4. A method according to claim 1, wherein said mammal is a primate.

5. A method according to claim 1, wh r in said antibody is a monoclonal antibody.

6. A method according to claim 1, wherein said antibody is an anti-PDGF-alpha receptor antibody.

7. A method according to claim 1, wherein said antibody is an anti-PDGF-beta receptor antibody.

8. A method according to claim 1, wherein said antibody is administered concurrently with, or within an antihyperplastically effective time period before, an occurrence of acute vascular injury in said mammal.

9. A method according t claim 8, wherein said injury is due to vascular reconstruction.

10. A method according to claim 9, wherein said vascular reconstruction comprises angioplasty, endarterectomy, reduction atherectomy, or anastomosis of a vascular graft.

11. A method according to claim 1, wherein said antibody is administered within an antihyperplastically effective time period following an occurrence of acute vascular injury in said mammal.

12. A method according to claim 11, wherein said injury is due to vascular reconstruction.

13. A method according to claim 12, wherein said vascular reconstruction comprises angioplasty, endarterectomy, reduction atherectomy or anastomosis of a vascular graft.

14. A method according to claim 1, wherein said antibody is administered concurrently with, or within an antihyperplastically effective time p riod before, emplacement of a vascular graft or transplanted organ.

15. A method according to claim 1, wherein said antibody is administered within an antihyperplastically effective time period following emplacement of a vascular graft or transplanted organ.

16. A method according to claim 1, wherein a panel of anti-PDGF recept r antib dies is administered to said mammal.

17. A method according to claim 16, wherein said panel f anti-PDGF recept r antibodies inhibits binding of AA, AB and BB isoforms of PDGF to PDGF receptors.

18. A method according to claim 16, wherein said panel of anti-PDGF receptor antibodies compris s anti-PDGF-alpha receptor antibodies and anti-PDGF-beta-receptor antibodies.

19. A method according to claim 1, wherein said antibody is a humanized monoclonal antibody.

20. A method according to claim 1, wherein said antibody is a single chain antibody.

21. A method according to claim 1, wherein said antibody is a chimeric antibody.

22. A method according to claim 21, wherein said antibody is a human-mouse chimeric antibody.

23. A method according to claim 22, wherein said chimeric antibody comprises mouse variable domains operably linked to human constant domains.

24. A method of inhibiting intimal hyperplasia at a site of vascular injury in a mammal, comprising:

administering to said mammal an anti-growth factor receptor antibody in an amount sufficient to inhibit at said site of injury an intimal hyperplastic process selected from the group consisting of vascular smooth muscle cell proliferation, vascular smooth muscle cell migration, and neointimal deposition of extracellular matrix, wherein said antibody inhibits a receptor function of said growth fact r r ceptor.

25. A method of inhibiting intimal hyperplasia in the vasculature of a mammal, comprising:

coordinately administering to said mammal an amount of a platelet derived growth factor (PDGF) antagonist and an amount of heparin, wherein said coordinately administered antagonist and heparin are combinatorially effective to inhibit said hyperplasia.

26. A method according to claim 25 wherein said PDGF antagonist is a non-peptidic PDGF antagonist.

27. A method according to claim 25 wherein said PDGF antagonist is an anti-PDGF receptor antibody.

28. A method according to claim 27, wherein said antibody and heparin are combinatorially effective to inhibit an intimal hyperplastic process selected from the group consisting of vascular smooth muscle cell proliferation, vascular smooth muscle cell migration, and neointimal deposition of extracellular matrix, at a site of vascular injury.

29. A method according to claim 27, wherein said antibody and heparin are administered sequentially.

30. A method according to claim 27, wherein said antibody and heparin are administered concurrently with, or within an antihyperplastically effective time period before, an occurrence of acute vascular injury in said mammal.

31. A method according to claim 30, wherein said injury is due to vascular reconstruction.

32. A method according to claim 31, wherein said vascular reconstruction comprises angioplasty, endovascular stenting, endarterectomy, endovascular laser

ablation, reduction atherectomy, or anastomosis of a vascular graft.

33. A method according to claim 27, wherein said antibody and heparin are administered within an antihyperplastically effective time period following an occurrence of acute vascular injury in said mammal.

34. A method according to claim 33, wherein said injury is due to vascular reconstruction.

35. A method according to claim 34, wherein said vascular reconstruction comprises angioplasty, endovascular stenting, endarterectomy, endovascular laser ablation, reduction atherectomy, or anastomosis of a vascular graft.

36. A method according to claim 27, wherein said heparin comprises a low molecular weight heparin having reduced antithrombotic activity.

37. A method according to claim 27, wherein said heparin comprises a heparan sulfate.

38. A method according to claim 27, wherein said antibody is a monoclonal anti-PDGF receptor antibody.

39. A method according to claim 27, wherein said antibody is an anti-PDGF-alpha receptor antibody.

40. A method according to claim 27, wherein said antibody is an anti-PDGF-beta receptor antibody.

41. A method according to claim 27, wherein said antibody is a humanized antibody.

42. A method according t claim 27, wherein said antibody is a singl chain antibody.

43. A method according to claim 27, wherein said antibody is a chimeric antibody.

44. A method according to claim 43, wherein said antibody is a human-mouse chimeric antibody.

45. A method according to claim 44, wherein said chimeric antibody comprises mouse variable domains operably linked to human constant domains.

46. A method according to claim 27, wherein a panel of anti-PDGF receptor antibodies is administered t said mammal.

47. A method according to claim 46, wherein said panel of anti-PDGF receptor antibodies inhibits binding of AA, AB and BB isoforms of PDGF to PDGF receptors.

48. A method according to claim 47, wherein said panel of anti-PDGF receptor antibodies comprises anti-PDGF-alpha receptor antibodies and anti-PDGF-beta receptor antibodies.

49. A method according to claim 27, wherein said mammal is a primate.

50. A method according to claim 27, wh rein said antibody and heparin are administered to said mammal by a mode of administration selected from the group consisting of intravascular, perivascular, transdermal and rectal administration modes.

51. A method according to claim 27, wherein said amount of antibody is a unit antibody dose of between approximately 0.1 μg and 100 mg of antibody per kilogram of body weight of said mammal per day.

52. A method according to claim 27, wherein said amount of antibody is a unit antibody dose of between approximately 50 μg and 20 mg of antibody per kilogram of body weight of said mammal per day.

53. A method according to claim 27, wherein said amount of antibody is a unit antibody dose of less than approximately 1 mg of antibody per kilogram of body weight of said mammal per day.

54. A method according to claim 27, wherein said amount of heparin is a unit heparin dose of between approximately 1 μg and 100 mg of heparin per kilogram of body weight of said mammal per day.

55. A method according to claim 27, wherein said amount of heparin is a unit heparin dose of between approximately 20 μg and 10 mg of heparin per kilogram of body weight of said mammal per day.

56. A method according to claim 27, wherein said administered amount of heparin is a unit heparin dose of less than approximately 1 mg of heparin per kilogram of body weight of said mammal per day.

57. A method according to claim 27, wherein said amount of antibody is a unit antibody dose of between approximately 0.5 μg and 10 mg of antibody per kilogram of body weight of said mammal per day, and wherein said amount of heparin is a unit heparin dose of between approximately 1 μg and 10 mg of heparin per kilogram of body weight of said mammal per day.

58. A method according to claim 27, wherein said amount of antibody is a unit antibody dose f between approximately 5 μg and 2 mg of antibody per kilogram of body weight of said mammal per day, and wherein said amount of heparin is a unit heparin d se of between approximately 50 μg and 1 mg of heparin per kilogram of body weight of said mammal per day.

59. A method according to claim 27, wher in said amount of antibody is administered in a combinatorially effective dose ratio, by weight, relative to said amount of heparin, between approximately .001:1 and 1,000:1.

60. A method according to claim 27, wherein said amount of antibody is administered in a combinatorially effective dose ratio, by weight, relative to said amount of heparin, between approximately .01:1 and 100:1.

61. A method according to claim 60, wher in said combinatorially effective dose ratio is between approximately .05:1 and 20:1.

62. A method according to claim 27, wherein said antibody is administrated in a bolus injection or infusion on a first day of an antibody treatment regimen, and wherein said antibody treatment regimen results in a minimum circulating level of said antibody in said mammal throughout an initial, three-day period of said treatment regimen of between approximately 20 μg and 1 mg of antibody per kilogram of body weight of said mammal.

63. A method acc rding t claim 62, wherein a circulating half-life of said antibody in said mammal is between approximately 12 hours and 14 days.

64. A method according to claim 27, wherein said antibody and heparin are administered concurrently with, or within an antihyperplastically effective time period before, emplacement of a vascular graft or transplanted organ.

65. A method according to claim 27, wherein said antibody and heparin are administered within an antihyperplastically effective time period following emplacement of a vascular graft or transplanted organ.

66. A method of inhibiting intimal hyperplasia at a site of vascular injury in a mammal, comprising:

coordinately administering to said mammal an amount of an anti-growth factor receptor antibody and an amount of heparin, wherein said antibody and heparin amounts are combinatorially effective to inhibit at said site of injury an intimal hyperplastic process selected from the group consisting of vascular smooth muscle cell proliferation, vascular smooth muscle cell migration, and neointimal deposition of extracellular matrix and wherein said antibody inhibits a receptor function of said growth factor receptor.

67. A pharmaceutical kit for use in treating intimal hyperplasia in the vasculature of a mammalian patient, comprising:

an anti-platelet derived growth factor (PDGF) receptor antibody in a pharmacologically suitable carrier; and

heparin in a pharmacologically suitable carrier.

68. A pharmaceutical kit according to claim 67, wherein said antibody and said heparin are precombined in a single carrier.

69. A pharmaceutical kit for use in a clinical treatment f intimal hyperplasia in th vasculature of a mammalian patient, comprising:

heparin; and

an anti-PDGF receptor antibody, wherein said heparin and said antibody are coordinately adminstrable to said patient by simultaneous, separate or sequ ntial delivery.